WAR MEDICINE

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A REPORT OF THIRTY CASES OF MENINGOCOCCIC CEREBROSPINAL MENINGITIS.

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Believing that a discussion of the clinical aspects of cerebrospinal meningitis might be of some value, we report a series of 30 cases that have been admitted and treated in the Base Hospital, Camp Pike, Arkansas, during November and December, 1917.

In the majority of instances the cases have been admitted within twelve to forty-eight hours after the appearance of symptoms, but a few were practically moribund at that time and died within a comparatively few hours. These, however, are included in the report.

For various reasons the meningitis patients have been turned over to the laboratory department, not only as regards diagnosis, but also treatment, a ward in the hospital being set aside for that purpose. The greatest part of the work has been done by Captain Morris and a much smaller amount by Captain Seehorn and Major McConnell.

SYMPTOMS ON ADMISSION. Although several of the patients were unconscious on admission, it was possible, as a rule, to elicit definite information concerning the subjective symptoms. In order of frequency they were as follows: (1) profound frontal headache; (2) stupor or coma; (3) rigidity of the neck; (4) vomiting; (5) Kernig's sign; (6) increased knee-jerks; (7) hyperesthesia; (8) slow pulse; (9) petechiæ; (10) slight increase in temperature. Strabismus was not present as an early symptom.

Headache. The headache was very severe in character, being much more marked than in typhoid fever, and nearly always was frontal. In one case in which it became basilar the patient lapsed into coma and finally died.

Mental Condition. In regard to the mental condition, there were all variations from an almost abnormal acuteness to complete coma. As a rule the patient was dull and inclined to sleep, but could be aroused, at which times he would appear irritable. Otherwise he would remain quiet, and breathing would be of a normal type, quite unlike that of the alcoholic, uremic or apoplectic.

Rigidity of the neck was, as a rule, well marked and accompanied by more or less retraction. In some instances this reached the point of a mild degree of opisthotonos. Any attempt at flexion, either active or passive, was painful, and evidently this rigidity was in no way due to the will of the patient. In this respect it differs from that seen in poliomyelitis, as in the latter the patient voluntarily resists, knowing that any motion will be painful. If this stiffness is not noticeable early it soon becomes very evident.

Vomiting occurred in about two-thirds of the cases and was of the projectile or cerebral type, coming without warning and without previous nausea. In a few of the cases it was the initial symptom.

Kernig's sign was positive in nearly every case, either slight or well marked, according to the general condition of the patient; but as it is found in various other infections, it is not of great diagnostic value. It was noted, however, that just at the moment when knee extension was made, after full flexion of the hip, both pupils dilate promptly and markedly. This same phenomenon was noted when flexion of the neck was attempted.

The knee-jerks were exaggerated in most of the cases, as were the plantar reflexes. Babinski's sign was absent in practically every case.

Hyperesthesia was present in many instances to a high degree and at times the skin showed marked irritability, as evidenced by positive "tâche cérébrale."

The pulse in nearly every case was slow, commonly between sixty and seventy, and not unusually it was in the fifties; as a rule a full volume, but occasionally irregular or intermittent, or both. The rate seemed to have little relation to the degree of temperature.

Petechiæ were present in but a small percentage of the cases, being marked in but three. Generally the distribution was diffuse, with variations in size and shape and not disappearing on pressure. In those showing well-marked petechiæ the other symptoms were severe, including a markedly purulent cerebrospinal fluid occurring in large amount, with a great increase in globulin.

Temperature. The temperature has not been high, particularly early in the disease. On admission the temperature was, as a rule, less than 101°, and even some of the worst cases did not go over 100.5°. The highest that was noted was 104.5°. except in one case in which it went up to 107° shortly before death. As compared with the English report the average temperature at the time of admission in our series was distinctly lower.

Various other symptoms were noted but did not appear with sufficient regularity to make them of diagnostic importance.

Strabismus of the convergent type was rather frequent.

Deafness was usually mild, but at times was well marked, was quite common, and generally persisted for a longer time than did the strabismus.

Herpes appeared in practically all of the cases and were abundant, usually most extensive on the lips at the mucocutaneous junction. The ears, nose and forehead were involved also. In several patients the herpes were so extreme that a good part of the face was covered by large scabs and the nose or an ear was swollen to twice its normal size.

The procedure in the cases was as follows: When the patient was admitted to the hospital he was seen by the medical officer, and if meningitis were suspected the laboratory was notified. A physical examination was made, and if it were decided to make a lumbar puncture the patient was sent to the meningitis ward. The skin over the junction of the fourth and fifth or third and fourth lumbar vertebræ was painted with iodin and a puncture made. If the patient were unconscious no anesthetic was used, as a rule. If slightly conscious and restless a mild chloroform anesthesia was employed. If fully conscious the patient was told what was to be done and no anesthetic was given. As a rule, general anesthesia was not used, as there seemed to be very little difficulty in removing considerable quantities of fluid, in one case as much as 125 c.c. On removing the stylet from the needle the first part of the fluid was allowed to flow into a sterile test-tube, then a small amount into a tube of culture media (serum dextrose agar). If the fluid were turbid the canal was allowed to drain and a dose of antimeningitis serum injected at once, the diagnosis being made later. It has happened in three instances that the cause of the condition was found to be the pneumococcus. These are not included in this series. Irrespective of the total amount of fluid removed, provided that it was more than 45 c.c., there was injected immediately 40 c.c. of serum. Whenever the quantity obtained was less than 45 c.c. the rule of injecting an amount of serum 5 c.c. less than that of the fluid withdrawn was followed.

If the spinal fluid were clear a globulin test and a cell count was made.

If either or both of these indicated a spinal irritation a dose of serum was given.

In regard to the pressure under which the fluid flowed it was observed that practically all the cases showed an increase, either moderate or marked. Inasmuch as an increased pressure was found in a number of cases that proved to be negative, this condition was disregarded as a positive indication for the injection of serum. Reliance was placed upon the character of the fluid, the presence of globulin and the cell count. The spinal fluid was centrifuged and the diagnosis confirmed by finding an abundance of polymorphonuclear leukocytes and a Gram-negative diplococcus. A positive diagnosis was made from the cultures on the basis of the appearance of the colonies and the finding of Gram-negative diplococci. Agglutination was not resorted to to determine the type of the organism on account of lack of personnel and of material. The fact that the cases with but very few exceptions showed improvement following the first injection of the antimeningitis serum would seem to indicate the correctness of the diagnosis.

In the examination of the sediment obtained by centrifuging the cerebrospinal fluid the organisms show the general morphology of the meningococcus. There was, at times, considerable variation in the size, shape and position in regard to the polymorphonuclear leukocytes. Most of the cocci were large "biscuit" shaped, arranged in pairs, as a rule, but sometimes like tetracocci. Others were smaller and more rounded. They were found both extra- and intracellularly, as has been reported by many investigators. Consequently not much weight was attached to location. Many appeared to be within the nuclei of the leukocytes. The organisms were uniformly Gram-negative. The number present varied greatly, some cases containing thousands, while in others, apparently of equal severity, it was with the greatest difficulty that any could be demonstrated. It was noted, as has been reported by the English Commission, that after the first injection the organisms were greatly diminished in those cases in which they had been numerous, and that after the second or third injection they could not be demonstrated.

In the more severe cases, when the fluid was allowed to stand for a short time, a diffuse gelatinous coagulum formed, this eventually settling to the bottom of the test-tube. The coagulum was very tenacious and could not be removed piecemeal. The uncoagulated part of the fluid remained cloudy, and on being centrifuged, pus cells and meningococci could be demonstrated.

ADMINISTRATION OF SERUM. In giving the serum the gravity method was not employed. Instead a Luer syringe of 40 c.c. capacity was used, there being a rubber tube with nipples for connection with the syringe and the needle. The serum was injected very slowly, but in many instances gave rise to more or less severe cramp-like pains in the lower extremities; these, however, were only temporary and did not require any treatment. It was very seldom that any untoward symptoms developed, the respirations continued without interruption and the pulse did not become rapid or weak. No attempts were made to follow Sophian's scheme of taking the blood-pressure at the time of injection.

In giving subsequent treatments the same methods were used and as much fluid as would readily flow was removed. The amount obtained varied greatly, the maximum amount being 150 c.c. and the minimum 5 c.c. Both these cases resulted fatally.

AMOUNT OF SERUM GIVEN AND FREQUENCY OF INJECTIONS. All of the cases, as soon as the lumbar puncture was done, and either a cloudy fluid discovered or a positive globulin obtained, were given, as a rule, 40 c.c. of serum. As already stated, the dose depending upon the amount of fluid withdrawn, in most instances the initial puncture yielded upward of 50 c.c. According to our experience it would appear unnecessary to give the serum more frequently than at twenty-four-hour intervals excepting in those fulminating forms when death seems imminent. One patient received four injections within thirty-six hours and showed improvement after each treatment. With but two or three exceptions the first three injections were given at twenty-four-hour intervals. The period between treatments was increased only when the temperature had been down to normal for at least thirty-six hours and when the last puncture had yielded a fluid decidedly less turbid than that obtained at the initial puncture. The globulin reaction (Noguchi method) also was used as a guide as to the time interval and prognosis. As the fluid became less turbid the globulin diminished relatively. Thus from a four-plus reaction at the first it would diminish, as a rule, so that by the third lumbar puncture the reaction would be one plus or less. Consequently, when the fluid decreased in turbidity, regardless of the amount obtained when the temperature had been normal for a minimum of thirty-six hours and when the globulin reaction came down to one plus or less, it seemed safe to wait forty-eight hours or perhaps longer before another injection was given. This depended, of course, as to whether or not any disturbing symptoms made their appearance.

Regarding the globulin reaction it was noted that the patient occasionally showed a marked improvement, yet the globulin did not go below two plus. At such times it is safe to disregard the globulin and wait forty-eight hours before treating. The persistence of the reaction may be due to the irritation of the serum or to the puncture itself.

Many of the cases will need no further serum after the fourth dose, yet it may be well to make a puncture at the end of forty-eight or seventy-two hours later to determine the pressure, the quality and quantity of the fluid and the globulin reaction. It might be recommended that in spite of the above findings being negative the patient be given another dose. In this connection it was observed that if after an interval of forty-eight or seventy-two hours another dose is given to a case that shows apparent recovery a violent reaction may occur. This reaction is far more severe than that following any previous injection. The temperature rises abruptly, the pulse increases markedly in rapidity and is occasionally irregular, pain in the back becomes acute and even a wild delirium has occurred. These symptoms subsided in from twelve to eighteen hours without any unpleasant sequelæ. In spite of the possibility of such a reaction it has been deemed advisable to give the additional injection.

If the patient does not show improvement it may be necessary to continue the lumbar punctures until recovery or death ensues. In one case, which finally proved fatal, twenty-three lumbar punctures were made.

The daily course of the disease showed interesting changes. Many of the patients were admitted, in a semicomatose condition that made it impossible to get any very clear statements. For that reason it was generally an easy matter to determine the effect of the serum by noting whether there was or was not any decrease in the stupor. Practically all of these cases showed signs of returning consciousness within six hours after the first injection. Within twelve hours nearly all could tell clearly events which took place up to the time of becoming unconscious, occasionally remembering some trivial occurrence during the period of coma. This happened even in four of the fatal cases.

The following signs of improvement were considered of value in the order given, and on them was based the prognosis of the case: (1) improvement in the consciousness of the patient; (2) fall in temperature to nearly normal; (3) diminution in intensity of headache; (4) no decrease or marked increase in the pulse rate; (5) no increase in the rigidity of the neck; (6) decrease in the globulin. It would seem that the early signs of improvement, those appearing within six hours after the first injection of the serum, are due, in part, to the fall of intracranial pressure, following the withdrawal of the large amount of cerebrospinal fluid. For this reason it does not seem advisable to base a favorable prognosis on very early improvement. If, however, the above-mentioned signs are still present at the end of twenty-four hours the probabilities are that the disease is yielding to the treatment. It must be remembered though that this form of cerebrospinal meningitis is a very capricious disease and must be watched carefully. If these indications of betterment were still present after twenty-four hours the improvement continued almost miraculously and with progressive rapidity. The favorable cases, by the end of thirty-six hours, became entirely conscious and were interested in what was being done for them. After this stage the temperature rarely rose above 101° and in most instances went no higher than 100°. All temperatures were rectal. The headache disappeared but the patients still had very vivid recollections of its terrific intensity. The pulse rate was usually about the same as on admission, or very slightly increased, generally of good quality and regular. Some of the cases, however, on admission had intermittent and irregular pulses. By this time the stiffness of the neck was less marked and the excruciating pain formerly present when attempts at flexion were made was absent. Some of the patients, even at this early stage, had complete lateral motion, with a fair degree of flexion.

As the favorable course continued it was within three to five days that most of the cases felt practically normal, except for a feeling of weakness, of which they all complained. This was most marked in the back and neck, probably due to the fact that the muscles of these regions had been contracted spasmodically for so long that more or less of the muscular tonicity had been lost.

The well-known observation that in practically all fevers an ascending pulse with a descending temperature is of bad prognostic import was emphasized in this series of meningitis. This was demonstrated very clearly in one of the fatal cases. He at first seemed to be doing as well as the others, yet his pulse rate increased progressively while his temperature decreased. He received twenty-three intraspinous inoculations of serum. This case terminated fatally.

No.	Initials.	Stage when treatment was begun. Approximate.	Number of lumbar punctures.	Amount of serum given.	Complications.	Period to convalescence or death.
1	J. O.	24 hours	7	205 c.c.	None	Oct. 31 to Nov. 7; cured.
2	J. F.	24 hours	11	320 c.c.	None	Nov. 8 to Nov. 18; cured.
3	J. V.	At least 18 hours	23	695 c.c.	None	Nov. 9 to Dec. 6; died.
4	F. F.	Admitted Oct. 29 Treated Nov. 11	16	440 c.c.	Broncho-pneumonia	27 days; died.
5	J. B.	24 hours	6	150 c.c.	None	Nov. 11 to Nov. 16; cured.
6	A. McM.	24 hours	23	555 c.c.	None	Nov. 11 to Dec. 8; cured.
7	H. D.	36 hours	5	125 c.c.	None	Nov. 12 to Nov. 15; cured.
8	F. J.	24 hours	6	155 c.c.	Orchitis	Nov. 13 to Nov. 20; cured.
9	G. M.	36 hours	7	110 c.c.	None	Nov. 15 to Nov. 29; cured.
10	F. S.	40 hours	10	210 c.c.	Orchitis	Nov. 16 to Dec. 11; cured.
11	L. D.	At least 24 hours	17	440 c.c.	Esophageal spasm	19 days; died.
12	M. H.	48 hours	15	345 c.c.	Esophageal spasm	Nov. 20 to Dec. 4; cured.
13	P. W.	24 hours	4	120 c.c.	None	Nov. 20 to Nov. 23; cured.
14	O. D.	48 hours	11	345 c.c.	None	Nov. 24 to Dec. 4; cured.
15	W. R.	5 days	1	40 c.c.	None	6 days; died.
16	J. T.	72 hours	5	120 c.c.	None	Dec. 3 to Dec. 8; cured.
17	G. S.	Over a week; low grade	4	105 c.c.	None	Dec. 2 to Dec. 8; cured.
18	A. W.	36 hours	8	200 c.c.	None	Dec. 4 to Dec. 12; cured.
19	C. M.	24 hours	4	110 c.c.	None	Dec. 7 to Dec. 10; cured.
20	J. H.	36 hours	5	120 c.c.	None	Dec. 9 to Dec. 16; cured.
21	W. B.	72 hours	4	140 c.c.	None	Dec. 14 to Dec. 17; cured.
22	R. P.	48 hours	1	40 c.c.	Anaphylaxis	Few hours; died.
23	R. W.	48 hours	5	135 c.c.	None	Dec. 16 to Dec. 20; cured.
24	M. J.	24 hours	5	110 c.c.	None	Dec. 18 to Dec. 22; cured.
25	J. S.	24 hours	3	90 c.c.	None	Dec. 20 to Dec. 22; cured.
26	W. C.	24 hours	3	75 c.c.	None	Dec. 20 to Dec. 22; cured.
27	W. R.	48 hours	2	40 c.c.	None	Dec. 23 to Dec. 25; died.
28	H. G.	24 hours	14	340 c.c.	None	Dec. 25 to Jan. 9; died.
29	C. H.	24 hours	5	140 c.c.	None	Dec. 25 to Jan. 1; cured.
30	A. W	24 hours	4	120 c.c.	None	Dec. 29 to Jan. 1; cured.

Complications. There were but two complications that made their appearance, orchitis and esophageal spasm. Orchitis occurred in two instances, one being unilateral and the other bilateral. The testicle involved was enlarged, and was extremely painful and tender. The epididymis, however, was not attacked. The process subsided under rest and the application of ice-caps. A venereal history was denied by both patients, and in neither were there any indications of any past or present trouble. In addition the absence of involvement of the epididymis would seem to favor the non-venereal character of the orchitis.

The other complication also appeared in 2 of the cases, both of which complained of difficulty in swallowing even liquids. In one of them the spasm cleared up very shortly without any special treatment. In the other the spasm persisted and attempts to feed by means of the stomach-tube were made. The first feeding was successful, but after that it became impossible to pass the tube into the stomach even under chloroform anesthesia. The tube would traverse about three inches of the esophagus, beyond which point it would not pass and would begin to coil upon itself. After several attempts were made a gastrostomy was performed. Twelve hours later the patient died, more from asthenia due to lack of nourishment than from the result of the operation or from marked pathological changes, due to the meningitis. Rectal feeding had been tried, but nothing was retained.

In addition to the above-mentioned complications certain other conditions developed in the course of the disease. The most common were serum sickness and urticaria. Most of the cases developed an urticaria in from seven to ten days after the first serum injection. In seeking for a cause for this late occurrence the conclusion was reached that the repeated intraspinous injections of serum gradually increase the permeability of the choroid plexus so as to allow the passage of the serum into the blood stream. That this process takes place on an extensive scale is evidenced by the fact that the urticaria produced is widespread and abundant. In this respect the action is interesting when compared with that of the intravenous injections of salvarsan, as with that there is very little, if any, passage of arsenic into the cerebrospinal fluid. Some of the herpes developed upon the urticarial wheals and thus produced a peculiar eruption.

So was stated in the British report, and as has been our experience, no symptoms of acute anaphylaxis have developed; the urticaria has been the only indication of active serum sickness. In one instance there was a very unfortunate occurrence. This patient was admitted in a moribund condition with his body covered by a diffuse petechial rash. He was given 40 c.c. of antimeningococcus serum immediately upon the removal of the spinal fluid. Three hours later it was decided, on account of the evident severity of the case, to give some serum intravenously. Forty cubic centimeters were given and within a few minutes after the withdrawal of the needle an acute superficial edema appeared, most noticeable in the eyelids, which rapidly became swollen, and within fifteen minutes the patient died from respiratory failure. At the time that it was decided to give the intravenous injection the question of anaphylaxis was considered, but in view of the fact that 40 c.c. of serum had been given intraspinously three hours before, without any disturbances occurring, it was decided to give the serum intravenously. This result substantiates the belief that it is not until repeated injections have been given that the choroid plexus becomes permeable.

So far as the autopsy reports are concerned there was comparatively little found; the findings were as follows:

CASE I.—J. J. V. Purulent meningitis, chiefly basilar, but some slight general involvement. Lateral ventricles contained an increased amount of fluid, quite turbid in appearance. Large amount of cerebrospinal fluid. Scattered areas of bronchopneumonia of right lower lobe, with slight purulent pleuritis. Pneumococci found in smear from pleura.

CASE II.—F. F., purulent meningitis. Large amount of fluid present. A few areas of purulent exudate over the frontal lobes. Fluid in ventricles slightly increased and cloudy. Bronchopneumonia and edema of both lungs, particularly the lower lobes. Small amount of slightly turbid fluid in the pericardium. Parenchymatous changes in the kidneys.

CASE III.—L. D. Basilar meningitis. Congestion and edema of both lungs.

Although this series does not comprise very many cases, yet the study of them has been of the greatest interest. The chief factor in regard to the prognosis is the period at which the treatment is begun. Under the conditions of civil life these cases are more likely to remain under observation for a day or two before the diagnosis is made and treatment instituted. At present when the probabilities of a case being meningitis are very great the cases come to the hospital much earlier. In fact, the suspected cases have outnumbered the true. The principle followed has been that it is much better to make a lumbar puncture and get negative results than to overlook a case. A number of patients showing well-marked symptoms of meningeal irritation have proved negative so far as meningitis is concerned, but several on further examination have shown the presence of pneumonia.

The treatment has been instituted in practically all the cases, just on the gross appearance of the fluid without waiting for any further confirmation of the diagnosis. It has also been evident that the conditions of the patient at the time of admission was not always a reliable ground on which to base the prognosis. Some of those who were in well-marked coma came out more rapidly and returned to normal more quickly than others who at first seemed less severely attacked.

As has been the experience generally, those who have recovered after receiving the serum treatment have remained entirely free from any sequelæ. Those who have been discharged as cured have not had a trace of any trouble, no interference with vision or hearing, nothing other than the general weakness following any severe disease.

In regard to the source of infection very little, in a way, has been determined. Eleven of the cases were received from two companies of two regiments that came to the cantonment from an infected section. In about a month it was apparently quiescent in these troops, then after a period of ten days another case developed, but for the past month there have been no further cases. Other cases were much more sporadic, coming from various regiments and companies scattered all around the Camp. In the case occurring in a nurse it was found that she had been taking care of a patient who subsequently developed meningitis. It is interesting to note, however, that both she and the patient developed the disease at practically the same time.

In conclusion it would seem that the important points are:

1. Early diagnosis.
2. Prompt treatment.
3. Persistent treatment.
4. Symptomatic treatment. Control of convulsions by bromides and chloral. Heart stimulants such as digitalein, strychnin and atropin also were used.

AMERICAN JOURNAL OF CARE FOR CRIPPLES.

THE current number of the *American Journal of Care for Cripples* maintains the level of war interest established by its predecessors since inauguration of the policy to include consideration of the military phases of the subject with which it deals.

THE FRENCH SYSTEM FOR RETURN TO CIVILIAN LIFE OF CRIPPLED AND DISCHARGED SOLDIERS. An important and substantial contribution in this issue is that by Major John L. Todd, C. A. M. C., under the above title. Major Todd takes pains to emphasize that the information at his disposal has been obtained from men or commissions